

CLAIMS

1. An oral pharmaceutical dosage form comprising pharmacologically effective amounts of an acid-susceptible proton pump inhibitor or a salt thereof and an H2 receptor antagonist or a salt thereof, and at least one pharmaceutically acceptable excipient(s) which results in a delayed release and/or extended release of the acid-susceptible proton pump inhibitor or the salt thereof, and said H2 receptor antagonist or the salt thereof is included in such a way that it is rapidly released from said dosage form.
- 10 2. The dosage form of claim 1, wherein the acid-susceptible proton pump inhibitor is selected from lansoprazole, omeprazole, pantoprazole, rabeprazole, pariprazole, leminoprazole, their pharmaceutically acceptable salts, enantiomers and salts of enantiomers.
- 15 3. The dosage form of claim 1 or 2, comprising from 1 mg to 100 mg of the acid-susceptible proton pump inhibitor or a salt thereof per single dose.
4. The dosage form of claim 1, wherein the H2 receptor antagonist is selected from cimetidine, ranitidine, nizatidine and famotidine, their pharmaceutically acceptable salts, isomers and salts of isomers.
- 20 5. The dosage form of claim 4, comprising from 1 mg to 800 mg of H2 receptor antagonist or salt thereof.
- 25 6. The dosage form of any one of claims 1-5, wherein the excipient(s) exerts the release controlling activity in the form of a membrane applied onto a core comprising the acid-susceptible proton pump inhibitor or a salt thereof, or in the form of a matrix system where the acid-susceptible proton pump inhibitor or a salt thereof is incorporated into the excipient(s).
- 30 7. The dosage form of any one of claims 1-6, wherein the H2 receptor antagonist or a salt thereof forms an outer layer applied onto a core comprising the acid-susceptible proton pump inhibitor or a salt thereof and excipients, wherein the core forms a matrix or

membrane system, capable of delayed and/or extended release of the acid-susceptible proton pump inhibitor or a salt thereof.

8. The dosage form of any one of claims 1-7, wherein the excipient(s) used to form

5 the membrane or matrix are inert or lipid.

9. The dosage form of claim 8, wherein the inert excipient(s) are non-polymeric-or polymeric materials such as calcium phosphate, ethyl cellulose, methacrylate copolymer, polyamide, polyethylene, polyvinyl alcohol or polyvinyl acetate.

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10. The dosage form of claim 8, wherein the lipid excipient(s) are non-polymeric-or polymeric materials such as carnauba wax, cetyl alcohol, hydrogenated vegetable oils, microcrystalline waxes, mono- and triglycerides, polyethylene glycol or polyethylene glycol monostearate.

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11. The dosage form of claim 9 or 10, wherein additional hydrophilic excipient(s) are used, such as alginates, carbopol, gelatin, hydroxypropyl cellulose, hydroxypropyl methylcellulose or methylcellulose.

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12. The dosage form of any one of claims 6-11, wherein an enteric coating layer is applied onto the membrane or matrix system and, optionally, a layer separating the enteric coating from the membrane or matrix system.

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13. The dosage form of any of claims 6-12, wherein an alkaline-reacting substance is admixed together with the acid-susceptible proton pump inhibitor or the salt thereof.

14. The dosage form of any one of claims 1-13, wherein said pharmacologically effective amounts are amounts capable to raise gastric pH to above 4 within two hours after administration and to keep it above 4 for at least 4 hours.

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15. The dosage form of claim 14, wherein said amounts are capable to keep gastric pH above 4 for at least 8 hours.

16. The dosage form of claim 14 or 15, wherein said pharmacologically effective amounts are amounts capable to raise gastric pH to above 3 within 2 hours from administration and to keep it above 3 for at least 4 hours.

5 17. The dosage form of claim 16, wherein said amounts are amounts capable to keep gastric pH above 3 for at least 8 hours.

18. The dosage form of any one of claims 1-17, comprising from 100 mg to 1000 mg of antacid agent and/or alginate.

10 19. The dosage form of claim 18, wherein the antacid agent comprises one or several of aluminum hydroxide, calcium carbonate, magnesium carbonate, basic magnesium carbonate, magnesium hydroxide, magnesium oxide, sodium hydrogen carbonate.

15 20. The dosage form of any one of claims 1-19, wherein the acid-susceptible proton pump inhibitor or a salt thereof and excipients, together forming a membrane or matrix system, are present in the form of a multiple-unit system consisting of a plurality of small units, consisting of pellets, granules or beads.

20 21. The dosage form of claim 20, wherein the small units in the multiple-unit system also contain an outer layer of a H2 receptor antagonist or a salt thereof.

22. The dosage form of claim 20, wherein the small units are dispersed in a H2 receptor antagonist or a salt thereof, optionally admixed with pharmaceutically acceptable excipients, such as disintegrant(s).

25 23. The dosage form of any one of claims 1-19, comprising two halves, one of which comprising an acid-susceptible proton pump inhibitor or a salt thereof in admixture with excipients capable of forming a matrix or membrane system and the other half comprising an H2 receptor antagonist or a salt thereof, optionally admixed with pharmaceutically acceptable excipients, such as disintegrant(s).

30 24. A capsule according to any one of claims 1-23.

25. A divided powder/pellet formulation according to any one of claims 1-23.
26. A tablet according to any one of claims 1-23.
- 5 27. The tablet of claim 26, being divisible.
28. The tablet of claim 26, being dispersible in water.
- 10 29. The tablet of claim 28, comprising a disintegrant.
30. A method for the manufacture of an oral pharmaceutical dosage form comprising pharmacologically effective amounts of an acid-susceptible proton pump inhibitor or a salt thereof and an H2 receptor antagonist or a salt thereof, and at least one pharmaceutically acceptable excipient which results in a delayed release and/or extended release of the acid-susceptible proton pump inhibitor or the salt thereof, and said H2 receptor antagonist or the salt thereof is included in such a way that it is rapidly released from said dosage form, said method comprising forming a first layer comprising said acid-susceptible proton pump inhibitor or salt thereof, and forming a coating thereon of said at least one excipient, and forming a second layer comprising said H2 receptor antagonist or salt thereof surrounding said first layer and said coating, and subsequently formulating the combined product of said first layer, said coating and said second layer into an oral pharmaceutical dosage form.
- 15 31. A method according to claim 30, wherein said acid-susceptible proton pump inhibitor is enclosed in said least one excipient, said excipient forming a lipid or water-insoluble matrix.
- 20 32. A method according to claim 30 or 31, wherein said first layer is formed to pellets, which are subsequently coated with said at least one excipient and are subsequently mixed with a carrier comprising said H2 receptor antagonist or salt thereof.
- 25 33. A method according to claim 32, wherein said carrier comprises a pharmacological disintegrant.

34. A method according to any one of claims 30-33, wherein said combined product is formulated into a tablet.

35. A method according to any one of claims 30-33, wherein said combined product is 5 formulated into a capsule capable of disintegrating in gastro-intestinal fluids.

36. A method according to any one of claims 30-35, wherein said oral pharmaceutical dosage form is provided with an enteric coating.

10 37. A method according to any one of claims 30-36, wherein said acid-susceptible proton pump inhibitor is selected from the group consisting of lansoprazole, omeprazole, pantoprazole, rabeprazole, pariprazole, lempiprazole and their pharmaceutically acceptable salts, enantiomers and salts of enantiomers.

15 38. A method according to any one of claims 30-36, wherein said H2 receptor antagonist is selected from the group consisting of cimetidine, ranitidine, nizatidine, famotidine and their pharmaceutically acceptable salts, isomers and salts of isomers.

20 39. Use of an oral pharmaceutical dosage form according to any one of claims 1-29, for the manufacture of a medicament for the treatment of conditions associated with the secretion of gastric acid.

40. Use of an oral pharmaceutical dosage form according to any one of claims 1-29 in association with one or more antibiotic agents for the eradication of *Helicobacter pylori*.

25 41. A method of treating a condition associated with the secretion of gastric acid, wherein an oral pharmaceutical dosage form according to any one of claims 1-29 is administered in a therapeutically effective amount to an individual human or animal afflicted with said condition.

30 42. A method for treating an infection by *Helicobacter pylori*, wherein an oral pharmaceutical dosage form according to any one of claims 1-29 in association with one or more antibiotic agents effective against *H. pylori* is administered in a therapeutically effective amount to an individual or human afflicted with said infection.

43. A method according to claim 41 or 42, wherein said oral pharmaceutical dosage form is administered concomitantly as two separate oral dosage forms, one comprising a pharmacologically effective amount of said acid-susceptible proton pump inhibitor or salt thereof, and the other comprising a pharmacologically effective amount of said H₂ receptor antagonist or salt thereof.

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44. A method according to any one of claims 41-43, comprising a dose regimen capable of maintaining gastric pH above 4 for at least 95% of a time period starting at 2 hours from the administration of the first dose and extending until 6 hours from the administration of the last dose.

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45. A method according to claim 44, wherein said time period is at least one week.

15 46. A method according to claim 44, wherein said time period is at least two weeks.

47. A method according to claim 44, wherein said time period is at least four weeks.

20 48. A method according to any one of claims 41-43, comprising a dose regimen capable of maintaining gastric pH above 3 for at least 95% of a time period starting at 2 hours from the administration of the first dose and extending until 6 hours from the administration of the last dose, in particular for at least four weeks.